

Treatment of Depression: A Comparative Study of E.C.T. and Six Drugs

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Since the introduction of drug therapy in depression, a wide range of pharmacological substances has been made available. It is possible to show that many of these substances are more effective than a placebo in the treatment of depression, but it is not an easy matter to evaluate them in relation to one another.

METHOD

In this trial the patients have been divided into two series of 100 patients each. Each series of 100 has been divided into groups of 25 by using Bradford Hill's System of Random Numbers, and each group has been given a specific treatment.

The treatments given were E.C.T., phenelzine ('Nardil'), imipramine ('Tofranil'), pheni-

prazine ('Cavodil'), amitriptyline ('Tryptizol'), 'Parstelin' and chlorprothixene ('Taractan').

In view of the fact that the number in each group was small (25), imipramine was given to a group in each series of 100 patients. This was used as a linking device and as a check on the reliability of the assessments made.

The patients were all female in-patients in a psychiatric hospital. Treatment was given for a period of three weeks only, since it is common practice to give E.C.T. for a period of three weeks. One investigator (D.S.) allocated the treatments by the Method of Random Numbers and supervised each individual patient. The other investigator (J.T.H.) assessed the degree of depression on admission, then again at weekly intervals for three weeks, so that four assessments were made. This was done on a four-point

TABLE I
Pharmacological Description of Drugs Used in the Trial

| | | Dosage |
|------------------------------|--|-----------------------------------|
| Imipramine ('Tofranil') | = N-(γ -dimethylaminopropyl)-iminodibenzyl hydrochloride .. | Up to 250 mg. daily. |
| 'Parstelin' | = Combination of: 'Parnate' 10 mg.=tranylcypromine sulphate; and 'Stelazine' 1 mg.=trifluoperazine hydrochloride .. | 1 tablet t.d.s. |
| Amitriptyline ('Tryptizol') | = 5-(3-dimethylaminopropylidene)-dibenzo (a,d) (1,4) cyclo-heptadiene hydrochloride | Up to 75 mg. t.d.s. |
| Pheniprazine ('Cavodil') | = Betaphenylisopropylhydrazine hydrochloride | 12 mg. daily |
| Phenelzine ('Nardil') | = Betaphenyl ethyl hydrazine | 15 mg. t.d.s. |
| Chlorprothixene ('Taractan') | = α -2-chloro-q(w-dimethyl aminopropylidene) thioxanthene .. | 120 mg. daily up to 180 mg. daily |

scale (0 to 3) on the following signs and symptoms:

TABLE II

| | |
|------------------------|-----------------------|
| Feelings of Depression | Suicidal Ideas |
| Retardation | Initial Insomnia |
| Agitation | Early Morning Waking |
| Ideas of Reference | Self-neglect |
| Ideas of Guilt or | Daily Mood Swing |
| Unworthiness | Hypochondriacal Ideas |
| Constipation | Loss of Appetite |

This investigator was quite unaware of the treatment which each patient had.

At the end of the trial the results were classified under each specific treatment, the total score before treatment was obtained and compared with the total score after treatment.

DISCUSSION

It is evident from this investigation that E.C.T. is still the most effective treatment for depression, while drugs such as imipramine and Parstelin are less effective to a significant degree, although they have a range of action which is significantly greater than that of a number of other drugs in common use in the treatment of depression. Of the other drugs described it has been shown, for example, that phenelzine is significantly superior to placebo in the treatment of depression (Hutchinson and Smedberg, 1960). Similarly Skarbek and Smedberg (1962) have demonstrated that amitriptyline is significantly superior to placebo in depressed patients.

Taractan is not in common use as an anti-depressive drug, but it was thought it would be of value in this trial in view of the work of Sargent and Dally (1962) on a related substance.

An attempt was made to evaluate each form of treatment in relation to specific symptoms on the lines suggested by Fleminger and Groden (1962), Kiloh *et al.* (1962). This was not of significant value apart from two symptoms, i.e. suicidal ideas and ideas of guilt or unworthiness.

In practically all the patients suicidal ideas vanished within one week of treatment, but this may well have been due to hospitalization. The rate of remission was greatest with E.C.T. and was obviously slower with drug therapy.

The commonest residual symptom was feelings of guilt or unworthiness and the following table shows the extent to which this persisted.

TABLE IV

Incidence of Ideas of Unworthiness After Treatment in Each Group of 25 Patients

| | Treatment | | | | | No. of Patients |
|-----------------|-----------|----|----|----|----|-----------------|
| E.C.T. | .. | .. | .. | .. | .. | 3 |
| Cavodil | .. | .. | .. | .. | .. | 8 |
| Imipramine (i) | .. | .. | .. | .. | .. | 9 |
| Imipramine (ii) | .. | .. | .. | .. | .. | 8 |
| Parstelin | .. | .. | .. | .. | .. | 9 |
| Phenelzine | .. | .. | .. | .. | .. | 11 |
| Amitriptyline | .. | .. | .. | .. | .. | 13 |
| Taractan | .. | .. | .. | .. | .. | 14 |

TABLE III

| Treatment | | | | | Total Score Before Treatment | Total Score After Treatment | % Recovery |
|-----------|------------------|----|----|----|---------------------------------|--------------------------------|---------------|
| 1. | E.C.T.* | .. | .. | .. | 547 | 73 | 86.7 |
| 2. | Imipramine (i)† | .. | .. | .. | 549 | 114 | 79.3 |
| | Imipramine (ii)† | .. | .. | .. | 525 | 142 | 73.0 |
| 3. | Parstelin† | .. | .. | .. | 501 | 125 | 75.1 |
| 4. | Amitriptyline | .. | .. | .. | 485 | 162 | 66.6 |
| 5. | Cavodil | .. | .. | .. | 548 | 214 | 61.0 |
| 6. | Phenelzine | .. | .. | .. | 568 | 234 | 58.9 |
| 7. | Taractan | .. | .. | .. | 486 | 204 | 58.1 |

* E.C.T. was significantly superior to all other treatments at $P < 0.05$ level.

† Imipramine and parstelin were significantly superior to treatments (4) to (7) at $P < 0.05$ level. (Chi-square tests of significance were used on the total scores to give these results.)

With the small numbers involved and the relatively short period of the trial, it is quite impossible to ascertain whether any particular treatment has a specific action on any one symptom of depression—apart from the obvious value of E.C.T. in dispersing ideas of unworthiness.

SUMMARY

Seven treatments for depression have been evaluated by a blind technique in a series of 200 female in-patients. It has been demonstrated that E.C.T. is significantly superior to all the other treatments, while imipramine and parstelin have been significantly more effective than amitriptyline, Cavodil, phenelzine and Taractan, which could all be regarded as com-

parable in action. The duration of each treatment was three weeks.

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